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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/686,529	10/16/2003	Homme W. Hellinga	GRT/1579-863	4003

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EXAMINER	
ZEMAN, ROBERT A	
ART UNIT	PAPER NUMBER
1645	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/05/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/686,529	HELLINGA ET AL.	
	Examiner	Art Unit	
	Robert A. Zeman	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 August 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-30* is/are pending in the application.

4a) Of the above claim(s) *16-30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9-6-06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The amendment and response filed on 8-23-2006 are acknowledged. Claims 1, 3, 5-8, 15, 18 and 22 have been amended. Claims 23-30 have been added.

Claims 1-30 are pending. Claims 16-22 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Newly submitted claims 23-30 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: the elected invention is drawn to a biosensor comprising a bacterial periplasmic binding protein and at least one reporter group wherein the newly added claims are drawn to multiple methods utilizing said biosensors.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 23-30 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claims 1-15 are currently under examination.

Information Disclosure Statement

The Information Disclosure Statement filed on 9-6-2006 has been considered. An initialed copy is attached hereto.

Claim Rejections Withdrawn

The rejection of claims 1 and 7, 8 and 15 rejected under 35 U.S.C. 112, second paragraph, as being rendered vague and indefinite by the use of the phrase "specific positions of said bPBP" is withdrawn in light of the amendment thereto.

The rejection of claim 1 rejected under 35 U.S.C. 112, second paragraph, as being rendered vague and indefinite by the recitation of the positions "10, 93, 149 and 183" is withdrawn in light of the amendment thereto.

The rejection of claim 4 rejected under 35 U.S.C. 112, second paragraph, as being rendered vague and indefinite by the use of the term "said ligand" is withdrawn in light of Applicant's arguments.

Claim Rejections Maintained

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

The rejection of claims 1-15 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-8 of U.S. Patent No. 6,277,627 is maintained for reasons of record.

Applicant argues:

1. U.S. Patent 6,277,627 does not exemplify any other bPBP other than GBP.

2. The only bPBP mentioned in the specification are GBP and MBP.

3. The claims of U.S. Patent 6,277,627 are limited to glucose binding proteins.

4. It would not have been obvious from claims 1-8 of U.S. Patent 6,277,627 to exclude glucose binding proteins and maltose binding proteins from the biosensors of instant claims 1-14.

5. Instant claim 15 is limited to biosensors with the reporter group attached to an endosteric site. The claims and specification of U.S. Patent 6,277,627 does not teach or suggest attachment of a reporter group to an endosteric site.

Applicant's arguments have been fully considered and deemed non-responsive.

With regard to Points 1-4, U.S. Patent 6,277,627 discloses that GBP is a member of a superfamily of receptor proteins and that their invention is not limited to the said "individual embodiments (see column 3, lines 31-37). Consequently, it would have been obvious to the skilled artisan to apply the teachings of U.S. Patent 6,277,627 to use other members of said receptor superfamily.

With regard to point 5, the specification of U.S. Patent 6,277,627 specifically discloses that the reporter groups can be within the ligand-binding pocket (i.e. can be an endosteric site) [see column 4, lines 21-22).

As outlined previously, although the conflicting claims are not identical, they are not patentably distinct from each other because both claims sets are drawn to biosensors comprising a bPGP and a reporter group wherein said reporter group is attached to the GBP and can constitute a fluorophore or a redox cofactor. Moreover, since the cited patented claims encompass all possible attachment positions within the GBP and the disclosure of the cited patent contemplates the same (see column 4-5), the specific positions recited in the instant claims are deemed to be obvious variations of the patented biosensors.

35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

The rejection of claims 1 and 3-15 under 35 U.S.C. 102(e) as being anticipated by Amiss et al. (US 2003/0134346) is maintained for reasons of record.

Applicant argues:

1. The reporting group is not permitted to be attached at position 149 of GBP in claim 1.

Applicant's arguments have been fully considered and deemed to be non-persuasive.

The disclosure of Amiss et al. does not limit the attachment of the reporter group to position 149 of the glucose binding protein. Amiss et al. disclose that the reporter groups may be attached **throughout the length of the galactose/glucose binding protein** including position (see paragraph 0034).

As outlined previously, Amiss et al. disclose biosensors comprising galactose/glucose binding proteins (GGBP) and reporter groups wherein said GGBP includes at least on mutation and at least one reporter group (paragraph 0017). Amiss et al. further disclose that mutations of binding proteins include the addition or substitution of cysteine groups, non-naturally occurring amino acids and replacement of substantially non-reactive amino acids with reactive amino acids to provide for the covalent attachment of electrochemical or photoresponsive reporter groups (see paragraph 0025) and that a variety of reporter groups can be used such as fluorophores and redox cofactors (see paragraph 0032)). Amiss et al. also disclose that said reporter groups can be attached to the GGBPs by any conventional means throughout the length of the protein including position 149 (see paragraph 0034). With regard to the to the specific $\Delta I_{std\ or}$ ΔR_{max} values recited in claims 11-14, it is deemed in the absence of evidence to the contrary, that since the biosensors disclosed by Amiss et al. are and those of the instant invention are the same they would necessarily have the same biochemical properties.

The rejection of claims 1 and 3-15 under 35 U.S.C. 102(e) as being anticipated by Amiss et al. (US Patent 6,855,556) is maintained for reasons of record.

Applicant argues:

1. The reporting group is not permitted to be attached at position 149 of GBP in claim 1.

Applicant's arguments have been fully considered and deemed to be non-persuasive.

The disclosure of Amiss et al. does not limit the attachment of the reporter group to position 149 of the glucose binding protein. Amiss et al. disclose that the reporter groups may be attached **throughout the length of the galactose/glucose binding protein** including position (see column 6 line 65 to column 7, line 8).

As outlined previously, Amiss et al. disclose biosensors comprising galactose/glucose binding proteins (GGBP) and reporter groups wherein said GGBP includes at least on mutation and at least one reporter group (column 3, lines 44-50). Amiss et al. further disclose that mutations of binding proteins include the addition or substitution of cysteine groups, non-naturally occurring amino acids and replacement of substantially non-reactive amino acids with reactive amino acids to provide for the covalent attachment of electrochemical or photoresponsive reporter groups (see column 5, lines 1-7) and that a variety of reporter groups can be used such as fluorophores and redox cofactors (see column 6, lines 55-59). Amiss et al. also disclose that said reporter groups can be attached to the GGBPs by any conventional means throughout the length of the protein including position 149 (see column 6 line 65 to column 7, line 8). With regard to the to the specific ΔI_{std} or ΔR_{max} values recited in claims 11-14, it is deemed in the absence of evidence to the contrary, that since the biosensors disclosed by Amiss et al. are and those of the instant invention are the same they would necessarily have the same biochemical properties.

35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The rejection of claims 1-15 under 35 U.S.C. 103(a) as being unpatentable over Hellinga (WO 99/34212 – IDS filed 3-14-2005) is maintained for reasons of record.

Applicant argues:

1. The instant invention is directed to biosensors in which at least one reporter group is attached at one or more amino acid positions of bacterial periplasmic binding protein (bPBP) wherein said amino acid sites are allosteric or endosteric sites and wherein the bPBP is not glucose binding protein (GBP) or maltose binding protein (MGP).

2. Hellinga does not teach or suggest attaching at least one reporter group to endosteric sites of a bPBP (Example 2) and the only bPBP disclosed having the reporter group attached to an

allosteric site is GBP. Consequently, the skilled artisan would not have the requisite expectation of success.

Applicant's arguments have been fully considered and deemed non-persuasive.

With regard to Point 2, Hellinga discloses that GBP is a member of a superfamily of receptor proteins and that their invention is not limited to the said "individual embodiments (see page 7, lines 11-14). Consequently, it would have been obvious to the skilled artisan to apply the teachings of Hellinga to use other members of said receptor superfamily with a reasonable expectation of success.

As outlined previously, Hellinga discloses biosensors comprising glucose binding proteins (GBP) and reporter groups wherein said GBP include mutations that allow site-specific introduction of the environmentally sensitive reporter group (see abstract). Hellinga further discloses that said reporter groups can be site-specifically introduced by total synthesis, semi-synthesis or gene fusion (see page 7, lines 18-19) and that a variety of reporter groups can be used a fluorophores and redox cofactors (see page 8 lines 3-7 and claims 4-5). Hellinga also discloses that said reporter groups can be positioned in the binding pocket (ligand binding pocket) or distally from the binding pocket (see page 9, line 13 to page 10, line14). Moreover, Hellinga discloses that the binding protein can be mutated either within the binding site or at allosteric sites (see page 10, lines 14-17).

The disclosure of Hellinga differs from the instant invention in that they don't specifically exemplify any other bPBP other than GBP. Moreover, they do not explicitly disclose the specific $\Delta I_{std\ or}$ ΔR_{max} values recited in claims 11-14.

However, Hellinga discloses that the strategy for introducing reporter groups into the exemplified GBP was successfully used with MBP and PBP. Consequently it would have been obvious to one of ordinary skill in the art at the time of the invention to apply the methods set forth by Hellinga in making GBP based biosensors to the making of biosensors comprising other periplasmic binding proteins. One would have had a reasonable expectation of success as Hellinga et al. disclose the ability to apply strategies to multiple periplasmic binding proteins.

With regard to the to the specific $\Delta I_{std\ or}$ ΔR_{max} values recited in claims 11-14, it is deemed in the absence of evidence to the contrary, that since the biosensors disclosed by Hellinga and those of the instant invention are the same they would necessarily have the same biochemical properties.

The rejection of claims 1-15 under 35 U.S.C. 103(a) as being unpatentable over Hellinga (U.S. Patent 6,277,627 – IDS filed 3-14-2005) is maintained for reasons of record.

Applicant argues:

1. The instant invention is directed to biosensors in which at least one reporter group is attached at one or more amino acid positions of bacterial periplasmic binding protein (bPBP) wherein said amino acid sites are allosteric or endosteric sites and wherein the bPBP is not glucose binding protein (GBP) or maltose binding protein (MGP).

2. Hellinga does not teach or suggest attaching at least one reporter group to endosteric sites of a bPBP (Example 2) and the only bPBP disclosed having the reporter group attached to an allosteric site is GBP. Consequently, the skilled artisan would not have the requisite expectation of success.

Applicant's arguments have been fully considered and deemed non-persuasive.

With regard to Point 2, Hellinga discloses that GBP is a member of a superfamily of receptor proteins and that their invention is not limited to the said "individual embodiments (see page 7, lines 11-14). Consequently, it would have been obvious to the skilled artisan to apply the teachings of Hellinga et al. to use other members of said receptor superfamily with a reasonable expectation of success.

Hellinga discloses biosensors comprising glucose binding proteins (GBP) and reporter groups wherein said GBP include mutations that allow site-specific introduction of the environmentally sensitive reporter group (see abstract). Hellinga further discloses that said reporter groups can be site-specifically introduced by total synthesis, semi-synthesis or gene fusion (see column 1, lines 46-48) and that a variety of reporter groups can be used a fluorophores and redox cofactors (see column 3, lines 48-52 and claims 4-5). Hellinga also discloses that said reporter groups can be positioned in the binding pocket (ligand binding pocket) or distally from the binding pocket (see column 4 lines 21-48). Moreover, Hellinga discloses that the binding protein can be mutated either within the binding site or at allosteric sites (see column 4, lines 49-53).

The disclosure of Hellinga differs from the instant invention in that they don't specifically exemplify any other bPBP other than GBP. Moreover, he does not explicitly disclose the specific ΔI_{std} or ΔR_{max} values recited in claims 11-14.

However, Hellinga discloses that the strategy for introducing reporter groups into the exemplified GBP was successfully used with MBP and PBP. Consequently it would have been

obvious to one of ordinary skill in the art at the time of the invention to apply the methods set forth by Hellinga in making GBP based biosensors to the making of biosensors comprising other periplasmic binding proteins. One would have had a reasonable expectation of success as Hellinga et al. disclose the ability to apply strategies to multiple periplasmic binding proteins.

With regard to the to the specific $\Delta I_{std\ or}$ ΔR_{max} values recited in claims 11-14, it is deemed in the absence of evidence to the contrary, that since the biosensors disclosed by Hellinga and those of the instant invention are the same they would necessarily have the same biochemical properties.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert A. Zeman whose telephone number is (571) 272-0866. The examiner can normally be reached on Monday- Thursday, 7am -5:30 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on (571) 272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov.

Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

ROBERT A. ZEMAN
PRIMARY EXAMINER
March 1, 2007